HOSPITAL PROFESSIONAL'S NEWBORN SCREENING UPDATE

Department of Health & Human Services
DHHS
NEBRASKA

Nebraska Newborn Screening Newsletter August 2014

Severe Combined Immune Deficiency(s) (SCIDs) to be added to Nebraska's newborn screening panel

Screening for Severe Combined Immune Deficiency (SCID) will begin in Nebraska with blood spots received at the screening lab on 10/04/2014. Screening for SCID more familiarly known to the lay public as "bubble boy disease" is currently done in 19 states.

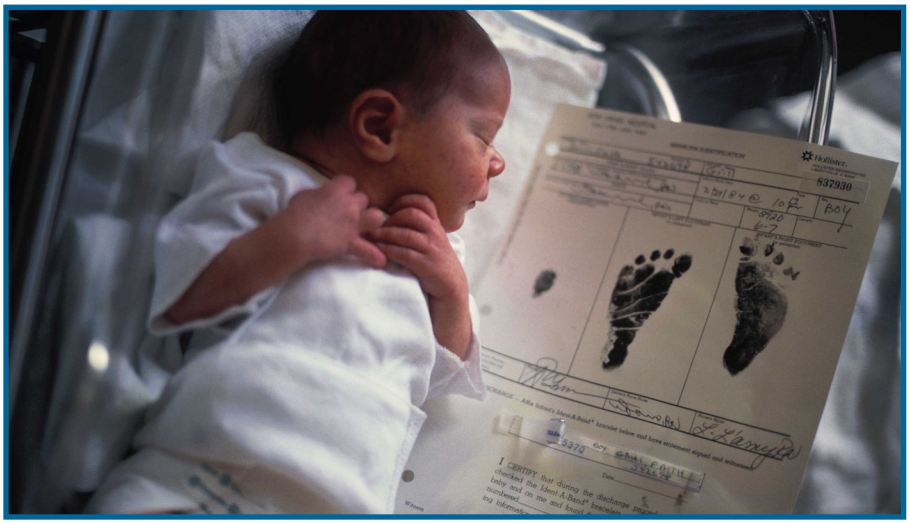
Following a National Institute of Health/Centers for Disease Control sponsored pilot in which over one million babies were screened, incidence rates were found to be higher than formerly believed. Classic SCID incidence is about 1:68,000, SCID Variants 1:68,000 and SCID + SCID Variants about 1:34,000. Hispanics have been found to have a higher incidence at about 1:22,000. Including all related T-cell deficiencies that are being detected by the screen, the incidence is about 1:22,000. A report of 11 states' experience with SCID screening is expected to be published in JAMA in the coming months.

Newborn screening for SCID has provided the opportunity to initiate treatment prior to symptoms for more babies. For babies with classic SCID who will receive a transplant, outcome is much better if it is achieved prior to infections and before three and half months of age. Rapid follow up with confirmatory testing is necessary to allow the babies with SCID and other T-cell deficiencies to be treated quickly and to ensure the best possible outcomes.

Read inside to find out how this addition will affect newborn nursery, laboratory and NICU practices at the hospital. .

" It is very exciting to have Nebraska start screening all newborns for this serious, but fortunately rare, genetic condition. Early detection is the key to successful therapy"

- Russell Hopp, DO
Pediatric Allergy/Immunologist



In This Issue

Survival with SCID in the 1970s meant living in isolation. Photo: David Vetter born without an effective immune system, made famous by the 1976 movie "The Boy in the Plastic Bubble." David died at the age of 12.

Thanks to research resulting in successful treatment and therapies, and earlier identification via the screening test, more babies live lives free of isolation. Patients with classic SCID can reconstitute their immune system with hematopoietic bone marrow stem cell transplant.

SCREENING TEST

The screening test for SCID is a measurement of the number of TRECs (T-cell receptor excision circles) formed during the maturation of T-cells. Pieces of DNA are lost during the recombination of T-cell receptor genes. These leftover pieces of DNA form into circles known as TRECs. The number of TRECs reflects the number of naïve T cells. Low copy numbers of TRECS indicate decreased T cell production which can indicate SCID. Other conditions with low T cell numbers may also be detected.

The screening test is done on a punch from the same dried blood spot specimen collected for the rest of the screening panel. Using Real-time Polymerase Chain Reaction (RT-PCR), the test detects copy numbers of TRECs. Zero or low TREC copy numbers are considered abnormal. When low TRECs are found, another test is run to determine adequacy of DNA amplification by running PCR on the sample for Beta Actin. If the results show low TRECs *and* low Beta Actin, it is considered i**nconclusive** due to failure of the DNA to amplify and a repeat dried blood spot is requested. Zero or very low copy numbers of TRECs (with adequate amplification as verified by Beta Actin) are indicative of Classic SCID or another variant or T-cell lymphopenia and are reported as **positive**. **Because of the risk of SCID, positive results on screening represent a medical emergency, as many will require transplant, enzyme therapy or gene therapy, and preventive steps should be followed to avoid exposure to sources of infection.**

The screening test is **highly sensitive and specific** in the full term newborn population. However the pre-term population tend to have more abnormal results because of the immaturity of the immune system and fewer T-cells being produced in the very early and early preterm births. We anticipate that most NICU admits with abnormal TRECs, will have normal results on the required repeat screens. This has been the experience of other programs. However we will be monitoring and tracking this as other states' repeat protocols may utilize different repeat screen time intervals. Heparin has been found to negatively affect the ability of PCR to amplify the DNA.. Therefore **do not collect the blood specimen using lines or other equipment (e.g. capillary tubes) that have been treated with heparin.** Excessive false positives or inconclusives are likely to result from exposure to heparin.

Ebrahim Shakir, MD

Russell Hopp, DO

Pediatric Immunologists in Nebraska who will work with primary care providers who have patients with positive SCID screening results to assist with diagnosis and treatment.

FOLLOW UP:

The Nebraska Newborn Screening Program (NNSP) in collaboration with the Advisory Committee and specialists have developed recommended follow-up activities for all probable situations including positive screens, inconclusive screens and situations where it appears the DNA failed to amplify. A newborn's physician will be provided with information including Parent Information (Fact) sheets, Physician Action (ACT) sheets, and recommendations for immediate next steps. For positive screens the baby's health care provider will be contacted by phone and connected with the Pediatric Immunologist on service that day. Nebraska's SCID Team has planned for rapid communication, confirmatory and diagnostic work up, and referral for transplant as needed. Hospital's Laboratory Directors will be receiving sample laboratory reports showing the format and language for various types of SCID screening results.

Since bone marrow stem cell transplant is so successful in newborns with Classic SCID who are transplanted *before the onset of any infection* and *by three and a half months of age*, rapid intervention to avoid exposure to sources of infection will be important when positive screen results are reported. Recommendations and consultation with one of the Pediatric Immunologists from the SCID team will be available to advise on this. One family's circumstances may be suitable for in-home protective isolation of the newborn, while another newborn's family situation might make hospital admission and protective isolation a better choice.

CONFIRMATORY TESTING:

Upon notification of a positive SCID result and consultation with the Pediatric Immunologist on call, the baby's primary healthcare provider will arrange the collection of blood for "Flow Cytometry, Immunodeficiency or SCID panel." Regional Pathology Services at the University of Nebraska Medical Center has developed this panel specifically for confirming newborns with positive SCID screen results. Testing is available Monday through Saturday, and specimens must be processed within 24 hours. Therefore **specimens should be collected *only* when they can be shipped to arrive the same day or overnight**. (i.e. don't collect confirmatory specimens for SCID on Saturdays).

Resources For Your Patients' Parents

Immune Deficiency Foundation – www.primaryimmune.org

Angels for Life Foundation - www.SCIDangelsforlife.com

American Academy of Allergy, Asthma and Immunology - www.aaaai.org

Nebraska Newborn Screening Pro-

Nebraska's SCID Team

Karen Eveans, MD will be the primary Follow-up Specialist from the Newborn Screening Program from whom you will receive initial notification of abnormal results, as well as supportive educational materials both professional and parent oriented. She will advise the baby's primary healthcare provider on ordering the confirmatory testing. She will follow-up with you and the SCID Team until diagnosis has been made and treatment or intervention as appropriate has been initiated. **Krystal Baumert, and Julie Luedtke** may also be contacting you. 402 471-0374

Ebrahim Shakir, MD 402 397-7400 or **Russell Hopp, DO** 402 354-4700 are the Pediatric Immunologists who will be the primary provider's first point of contact after hearing from the newborn screening program. They will consult on next steps and interpreting the flow cytometry. Referrals to these specialists may be in order after flow cytometry is complete for further diagnosis and treatment plan.

James L. Harper, MD, Pediatric Hematologist, will work with the team to facilitate donor match and bone marrow stem cell transplant as needed.

Samuel Pirruccello, MD, UNMC Regional Pathology Services, has developed the Flow Cytometry, Immunodeficiency or SCID Panel including appropriate subspecies, specifically to help in the diagnosis of positive SCID screens.

Special Instructions - Specimen Collection for Confirmatory Testing by Flow Cytometry

In the State of Nebraska the Flow Cytometry – SCID panel can be obtained at Regional Pathology Services at UNMC in Omaha, NE. **Careful coordination** for adequately obtaining the specimen and transporting it to UNMC is required.

Please keep the following information in mind when coordinating this process.

- Baby should **not be exposed** to sick people during this process.
- The specimen should arrive at the testing lab **within 24 hours of collection**
- Testing is available Monday through Friday from 8:00 AM – 5:00 PM. Testing is also done on Saturdays as staff is there in the morning through early afternoon when work is completed.

Both the collecting lab and the flow cytometry lab need to be contacted to ensure that appropriate personnel are available.

The number for the **Flow Laboratory is (402) 559-7787. Regional Pathology Services can also be contacted at (402) 559-6420.** Contacting the lab to alert them to the planned collection is especially necessary for any specimens that will be arriving on Saturday.

When alerting the collection laboratory, make sure that appropriate staff for collection will be available, that a courier will be available to transport the specimen in a timely manner and that information is given to staff about infection control. Advise the staff that the baby needs to avoid exposure to infectious diseases and should not be waiting in an area where this can occur.

Flow Cytometry, SCID panel should be ordered. If the baby has not had a CBC, this needs to be done as well. The CBC results should be sent to the flow cytometry lab as soon as they are available.

Specimen collected should be 1.0 cc of blood.

The preferred specimen is a heel stick venous collection into a capillary tube with EDTA (then transferred to a purple top micro-container). The collection site **must not be squeezed to get the blood flowing** as it will damage the white cells to some degree.

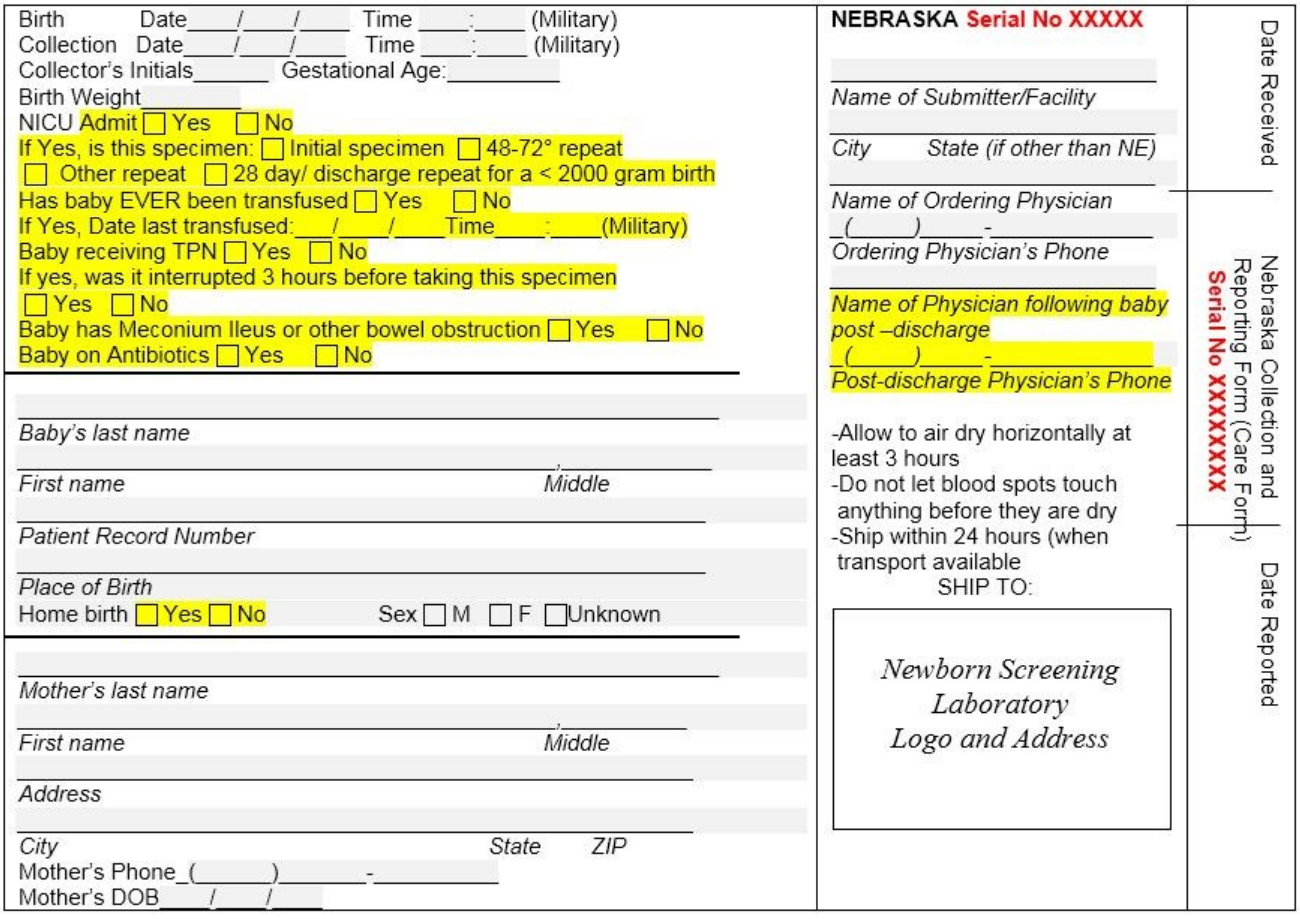
For **shipping** the specimen should be handled like a CBC specimen is ordinarily handled. The specimen needs to be maintained at or near room temperature. The specimen needs to **arrive at the flow laboratory within 24 hours of collection**.

BLOOD-SPOT FILTER PAPER COLLECTION DEVICE CHANGES

Revisions (highlighted in yellow) are designed to obtain improved demographic data. Yes/No answers provide clarity as to how to complete the form. New to the form is the information about the name and phone number of the physician who will be following the baby post-discharge. It is hoped that by completing this information fewer follow-up phone calls will need to be made to birthing facilities to gather that information, and fewer delays in communicating to the right healthcare provider when follow up is needed. Facilities will be provided with this new form when old stock has been depleted.

Heparin and PCR

The use of heparin in some devices used to collect blood can reduce the ability of PCR to amplify the DNA. One way to distinguish between a positive screen and a result that is likely showing low TRECs due to amplification problems, is the reflex test to look for Beta Actin. When both TRECs and Beta Actin are low, the screening lab won't be alerting the provider of a possible Positive SCID screen. Rather, they will be requiring a repeat dried blood spot specimen, in order to obtain a reliable screen result. Avoiding heparin, can reduce the number of repeats needed, and avoid a possible delayed diagnosis for a true positive.



Birth Date____/____/____ Time ____:____ (Military)
Collection Date____/____/____ Time ____:____ (Military)
Collector's Initials_____ Gestational Age:_____
Birth Weight_____
NICU Admit ☐ Yes ☐ No
If Yes, is this specimen: ☐ Initial specimen ☐ 48-72° repeat
☐ Other repeat ☐ 28 day/ discharge repeat for a < 2000 gram birth
Has baby EVER been transfused ☐ Yes ☐ No
If Yes, Date last transfused:___/____/____Time____:____(Military)
Baby receiving TPN ☐ Yes ☐ No
If yes, was it interrupted 3 hours before taking this specimen
☐ Yes ☐ No
Baby has Meconium Ileus or other bowel obstruction ☐ Yes ☐ No
Baby on Antibiotics ☐ Yes ☐ No

Baby's last name
First name Middle
Patient Record Number
Place of Birth
Home birth ☐ Yes ☐ No Sex ☐ M ☐ F ☐ Unknown

Mother's last name
First name Middle
Address
City State ZIP
Mother's Phone_(_____)_____-_____
Mother's DOB____/____/____

NEBRASKA Serial No XXXXX

Name of Submitter/Facility
City State (if other than NE)
Name of Ordering Physician
_(_____)_____-_____
Ordering Physician's Phone
Name of Physician following baby post –discharge
_(_____)_____-_____
Post-discharge Physician's Phone

-Allow to air dry horizontally at least 3 hours
-Do not let blood spots touch anything before they are dry
-Ship within 24 hours (when transport available
SHIP TO:

Newborn Screening Laboratory Logo and Address

Date Received
Nebraska Collection and Reporting Form (Care Form)
Serial No XXXXXXX
Date Reported

Calling all hospital QA/QI experts…we want your input!

The Quarterly Quality Assurance Reports of hospital performance on various metrics associated with newborn screening are undergoing revision. We want to be sure these are meaningful and helpful to facilities. One enhancement will be that hospitals will have the ability to run their own reports from the PerkinElmer Genetics Web-portal.

Metrics that are measured in a manner more consistent with nationally recommend measures should help us compare our performance with other states. For example one current recommended measure is: The percent of initial specimens received at the lab within 24 hours of collection. However we currently only measure the "average" time for initial specimens to arrive at the lab (as well as averages for all the other turn-around event time frames. Changing the measure to look at the number and percent of specimens that arrive within a pre-determined time frame as a benchmark gives us a better measure on which to target improvement efforts.

The measures that are currently being considered by the Secretary's Discretionary Committee on Heritable Diseases in Newborns and Children in response to the "timeliness" concerns are:

- Percent of initial specimens collected between 24-48 hours of birth.
- Percent of initial specimens received at the lab within 24 hours of collection.
- Percent of specimens with critical results reported within 5 days of birth.
- Percent of all specimens with results reported out within 5 days of collection.

Please contact Julie Luedtke, Program Manager 402 471-6733 or Julie.luedtke@nebraska.gov with ideas, or if you're interested in serving on a sub-committee to address NBS quality assurance measures for hospitals.

Contact Us

Give us a call for more information or questions about SCID or newborn screening.

Nebraska Newborn Screening Program–DHHS
301 Centennial Mall South
Lincoln, NE 68509-5026

(402) 471-0374

Newbornscreening@nebraska.gov

Visit us on the web at www.dhhs.ne.gov/nsp

Newborn Screening Program
Nebr. Dept. of Health & Human Svs.
301 Centennial Mall South
Lincoln, NE 68509-5026

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